

# Antiepileptic Drugs for Epilepsy

## EDUCATIONAL OBJECTIVES

After completing this activity, participants should be better able to:

1. Define the difference between a seizure and epilepsy.
2. Identify causes and risk factors associated with epilepsy.
3. Understand the proposed pathophysiology of seizures.
4. Describe the mechanism of action of AEDs used in the management of epilepsy.
5. Assess adverse effects and potential drug-drug interactions associated with the use of AEDs

## CE EXAM RATIONALE

### 1. Epilepsy is:

- A. The most common neurologic disorder worldwide
- B. A chronic condition in which patients experience recurrent, unprovoked seizures\*\*\*
- C. An isolated event resulting from abnormal electrical disturbances in the brain
- D. Not classified based on seizure type

### Correct answer: B

*Epilepsy is defined as a chronic condition in which patients experience recurrent, unprovoked seizures that range from short-lived intervals of inattention or muscle jerking to severe and elongated convulsions. It is the fourth most common neurologic disorder, affecting approximately 65 million people worldwide. The International Classification of Epileptic Seizures classifies seizures as partial (focal) or generalized.*

### 2. Possible causes of epilepsy and seizures include:

- A. Stroke
- B. Head trauma
- C. Medications such as antidepressants and antipsychotics
- D. All of the above\*\*\*

### Correct answer: D

*The cause of epilepsy is idiopathic in origin in approximately half of all patients. However, several medical conditions have an associated risk or causation with epilepsy, including traumatic brain injury (TBI), CNS infections, hypoglycemia, eclampsia, fever, and stroke. In addition, many medications have been associated with precipitating seizures (Table 1).*

### 3. Mechanisms of seizure control include all of the following except:

- A. GABA enhancement
- B. Sodium channel blockade

C. Calcium channel blockade

D. Sodium channel enhancement\*\*\*

**Correct answer: D**

*A number of agents have proven to be beneficial in the management of seizures by potentiating and preventing the reuptake or metabolism of GABA. Various medications, including sodium channel blockers, target inactivated (closed) sodium channels and provide utility in seizure management. Ethosuximide acts by increasing seizure threshold and suppressing paroxysmal spike-and-wave patterns in absence seizures through T-type calcium channel blockade.*

**4. TS is a 51-year-old patient with newly diagnosed psychomotor seizures and medical history significant for QT prolongation. Which antiepileptic drug (AED) may be useful in the treatment of TS?**

A. Primidone\*\*\*

B. Rufinamide

C. Felbamate

D. Valproic acid

**Correct answer: A**

*Primidone is indicated for generalized tonic-clonic, psychomotor, and focal seizures. Selected cases have shown that primidone may also be beneficial in patients with QT prolongation and coexisting seizure activity. Rufinamide is contraindicated in patients with familial short QT syndrome at doses >2,400 mg. Felbamate is indicated for refractory seizures. While valproic acid is widely used, its unfavorable side-effect profile is undesirable for many patients.*

**5. CYP450 enzyme inducers include all of the following AEDs except:**

A. Phenytoin

B. Carbamazepine

C. Brivaracetam\*\*\*

D. Phenobarbital

**Correct answer: C**

*Although the exact mechanism of anticonvulsant activity is unknown, brivaracetam is thought to reduce seizure frequency by binding to synaptic vesicle protein 2A (SV2A) in the brain similar to that of levetiracetam. Many of the commonly prescribed anticonvulsants are known CYP450 enzyme inducers, including carbamazepine, eslicarbazepine, oxcarbazepine, fosphenytoin, perampanel, phenytoin, phenobarbital, primidone, and topiramate ( $\geq 200$  mg/day).*

**6. Which of the following benzodiazepines is *not* indicated for treatment of status epilepticus?**

- A. Diazepam
- B. Clonazepam\*\*\***
- C. Lorazepam
- D. Midazolam

**Correct answer: B**

*Clobazam is indicated for adjunct therapy in Lennox-Gastaut syndrome. Diazepam, lorazepam, and midazolam are typically reserved for status epilepticus. To date, lorazepam and diazepam are preferred options in status epilepticus and have no significant differences in effectiveness, while IM midazolam has shown superior effectiveness compared to IV lorazepam in adults with convulsive status epilepticus without established IV access.*

**7. IV phenytoin administration is not to exceed what rate to avoid risk of infusion-related cardiovascular events?**

- A. 50 mg/min\*\*\***
- B. 60 mg/min
- C. 70 mg/min
- D. 80 mg/min

**Correct answer: A**

*In contrast to the oral formulation, IV phenytoin has been known to precipitate infusion-related adverse cardiovascular effects at rates >50 mg/min. Peripheral catheter administration results in pain, necrosis, and, less commonly, “purple glove syndrome” (i.e., skin disease in which the extremities become swollen, discolored, and painful). Rate reduction to <50 mg/min and the use of large-gauge catheters is effective in preventing tissue damage attributed to IV phenytoin.*

**8. Carbamazepine, oxcarbazepine, and eslicarbazepine have the potential to cause what adverse effect?**

- A. Weight gain
- B. Atrial fibrillation
- C. Alopecia
- D. SIADH\*\*\***

**Correct answer: D**

*In relation to its adverse-effect profile, syndrome of inappropriate antidiuretic hormone secretion (SIADH) has been observed in up to 21.7% of patients utilizing high doses of carbamazepine (1,200 mg/day). Although associated with a similar side-effect profile to that of carbamazepine, in some instances oxcarbazepine poses a greater risk for hyponatremia and SIADH as compared to carbamazepine. SIADH has been observed in as few as 3% of patients using eslicarbazepine compared to the higher percentages in oxcarbazepine and carbamazepine.*

**9. Vigabatrin carries a black box warning for what potential adverse effect?**

- A. Hepatic failure
- B. Serious skin reactions
- C. Permanent vision loss\*\*\*
- D. Aplastic anemia

**Correct answer: C**

*Vigabatrin carries a black box warning for permanent vision loss, which increases with increasing dose and cumulative exposure. Visual exams are recommended prior to initiation, every 3 months during, and 3 to 6 months after treatment. For this reason, vigabatrin is only available through the Sabril REMS program, which states that providers and pharmacies must be certified to prescribe and dispense.*

**10. Phenobarbital is contraindicated in patients with which of the following conditions?**

- A. An obstructed airway\*\*\*
- B. Status epilepticus
- C. HLA-B\*1502 positive
- D. Generalized tonic-clonic seizures

**Correct answer: A**

*Phenobarbital is a schedule IV controlled substance indicated for status epilepticus, generalized tonic-clonic seizures, and partial seizures. In the treatment of status epilepticus, IV phenobarbital is indicated as first-line treatment when IV benzodiazepines are not available. It is also important to be aware that extravascular administration of phenobarbital should be avoided due to the risk of necrosis. Additionally, patients with airway obstruction should avoid use due to the increased risk of severe respiratory depression and dyspnea.*